

WHAT IS CLAIMED IS:

1 1. A method for the manufacture of a pharmaceutical tablet which upon
2 oral ingestion delivers a first drug by immediate release and a second drug by prolonged
3 release defined as a release rate into gastrointestinal fluid that is slow enough to leave at least
4 about 40% of said second drug unreleased one hour after ingestion, said method comprising:

5 (a) dispersing said second drug in a solid matrix to form a unitary body which
6 upon immersion in gastrointestinal fluid releases said second drug by prolonged
7 release;

8 (b) depositing on a surface of said unitary body a polymeric film that is
9 devoid of either said first drug or said second drug;

10 (c) depositing over said polymeric film a fluid medium comprising said first
11 drug and a liquid carrier that does not remove said polymeric film upon contact
12 therewith; and

13 (d) evaporating said liquid carrier from said fluid medium thus deposited to
14 leave a solid layer containing said first drug over said unitary body.

1 2. The method of claim 1 in which said solid matrix is a member selected
2 from the group consisting of celluloses, substituted celluloses, microcrystalline cellulose,
3 polysaccharides, substituted polysaccharides, poly(alkylene oxide)s, poly(vinyl alcohol),
4 starch, starch-based polymers, crosslinked poly(acrylic acid)s, and substituted crosslinked
5 poly(acrylic acid)s.

1 3. The method of claim 1 in which said solid matrix is a member selected
2 from the group consisting of poly(ethylene oxide), hydroxypropyl methyl cellulose, and
3 combinations of poly(ethylene oxide) and hydroxypropyl methyl cellulose.

1 4. The method of claim 1 in which said polymeric film is a member
2 selected from the group consisting of poly(ethylene oxide), hydroxypropyl methyl cellulose,
3 polyvinyl alcohol, combinations of poly(ethylene oxide) and hydroxypropyl methyl cellulose,
4 and combinations of polyvinyl alcohol and poly(ethylene oxide).

1 5. The method of claim 1 in which said fluid medium comprises a liquid
2 solution of said first drug in a solvent.

1 6. The method of claim 1 in which said fluid medium comprises a liquid
2 solution of said first drug and a polymer in a solvent.

1 7. The method of claim 1 in which said fluid medium comprises a
2 suspension of said first drug in solid particle form in a liquid suspending agent.

1 8. The method of claim 1 in which said fluid medium comprises a
2 suspension of said first drug in solid particle form and a dispersing agent, also in solid
3 particle form, in a liquid suspending agent, said dispersing agent being a substance that
4 separates into discrete particles upon contact with gastrointestinal fluid.

1 9. The method of claim 1 in which said fluid medium is an aqueous
2 suspension of said first drug, and said first drug is comprised of particles having a weight-
3 averaged diameter equal to or less than 25 microns.

1 10. The method of claim 1 in which said fluid medium is an aqueous
2 suspension of said first drug, and said first drug is comprised of particles having a weight-
3 averaged diameter equal to or less than 10 microns.

1 11. The method of claim 1 in which the weight ratio of said polymeric film
2 to said unitary body is from about 0.005:1 to about 0.2:1.

1 12. The method of claim 1 in which the weight ratio of said polymeric film
2 to said unitary body is from about 0.01:1 to about 0.1:1.

1 13. The method of claim 1 in which the weight ratio of said polymeric film
2 to said unitary body is from about 0.01:1 to about 0.08:1.

1 14. The method of claim 1 in which (b) comprises surrounding said unitary
2 body entirely with said polymeric film, and said solid layer of (d) is a shell completely
3 encasing said unitary body and polymeric film.

1 15. The method of claim 1 in which (b) and (c) comprise depositing said
2 polymeric film and said first drug over only a portion of the entire surface of said unitary
3 body, leaving the remainder of said unitary body exposed.

1 16. The method of claim 1 in which said liquid carrier of step (c) is water.

1 17. The method of claim 1 in which said liquid carrier of step (c) is an
2 organic solvent.

1 18. The method of claim 17 in which said organic solvent is a member
2 selected from the group consisting of ethanol, hexanes, chloroform, carbon tetrachloride, and
3 dimethyl sulfoxide.

1 19. A dosage form for delivering a first drug that is immediately releasable
2 upon ingestion and a second drug that is releasable by prolonged release defined as a release
3 rate that is slow enough to leave at least about 40% of said second drug unreleased one hour
4 after ingestion, said dosage form comprising:

5 a prolonged-release section comprising said second drug dispersed in a solid
6 matrix that releases said second drug by prolonged release upon immersion of said
7 dosage form in gastrointestinal fluid;

8 a polymeric film adhering to a surface of said prolonged-release section, said
9 polymeric film being penetrable by gastrointestinal fluid and devoid of both said first
10 drug and said second drug; and

11 an immediate-release section comprising a solid layer adhering to said
12 polymeric film, said solid layer comprising said first drug dispersed in a matrix that
13 promotes immediate release of said first drug upon immersion of said dosage form in
14 gastrointestinal fluid.

1 20. The dosage form of claim 19 in which said solid matrix is a member
2 selected from the group consisting of celluloses, substituted celluloses, microcrystalline
3 cellulose, polysaccharides, substituted polysaccharides, poly(alkylene oxide)s, poly(vinyl
4 alcohol), starch, starch-based polymers, crosslinked poly(acrylic acid)s, and substituted
5 crosslinked poly(acrylic acid)s.

1 21. The dosage form of claim 19 in which said solid matrix is a member
2 selected from the group consisting of poly(ethylene oxide), hydroxypropyl methyl cellulose,
3 and combinations of poly(ethylene oxide) and hydroxypropyl methyl cellulose.

1 22. The dosage form of claim 19 in which said polymeric film is a member
2 selected from the group consisting of poly(ethylene oxide), hydroxypropyl methyl cellulose,

polyvinyl alcohol, combinations of poly(ethylene oxide) and hydroxypropyl methyl cellulose, and combinations of polyvinyl alcohol and poly(ethylene oxide).

23. The dosage form of claim 19 in which said solid matrix of said unitary body is defined as a first solid matrix and said fluid medium comprises said first drug in particle form and a second solid matrix, also in particle form, said second solid matrix being a substance that separates into discrete particles upon immersion in gastrointestinal fluid.

24. The dosage form of claim 19 in which the weight ratio of said polymeric film to said unitary body is from about 0.005:1 to about 0.2:1.

25. The dosage form of claim 19 in which the weight ratio of said polymeric film to said unitary body is from about 0.01:1 to about 0.1:1.

26. The dosage form of claim 19 in which the weight ratio of said polymeric film to said unitary body is from about 0.01:1 to about 0.08:1.

27. The dosage form of claim 19 in which said polymeric film and said immediate-release section constitute a shell that fully encases said prolonged-release section.

28. The dosage form of claim 19 in which said polymeric film and said immediate-release section cover a portion of the surface of said prolonged-release section, leaving the remainder of said prolonged-release section exposed.

29. The dosage form of claim 19 in which one of said first and second drugs is a diuretic and the other is a member selected from the group consisting of angiotensin converting enzyme inhibitors and angiotensin II antagonists.

30. The dosage form of claim 29 in which said diuretic is a loop diuretic.

31. The dosage form of claim 30 in which said loop diuretic is a member selected from the group consisting of furosemide, torsemide, ethacrynic acid, and bumetanide.

32. The dosage form of claim 29 in which said diuretic is a thiazide diuretic.

1 **33.** The dosage form of claim **34** in which said thiazide diuretic is a
2 member selected from the group consisting of chlorothiazide, bendoflumethazide,
3 hydroflumethazide, trichlorthiazide, chlorthalidone, indapamide, metolazone, quinethazone
4 and hydrochlorthiazide.

1 **34.** The dosage form of claim **29** in which said diuretic is a potassium-
2 sparing diuretic.

1 **35.** The dosage form of claim **34** in which said potassium-sparing diuretic
2 is a member selected from the group consisting of amiloride hydrochloride and triamterene.

1 **36.** The dosage form of claim **19** in which said first drug is a member
2 selected from the group consisting of lisinopril and losartan, and said second drug is a
3 diuretic.

1 **37.** The dosage form of claim **19** in which said first drug is a glitazone, and
2 said second drug is metformin hydrochloride.

1 **38.** The dosage form of claim **19** in which said first drug is pyridoxine
2 hydrochloride, and said second drug is a member selected from the group consisting of
3 atorvastatin, simvastatin, pravastatin, lovastatin, cerivastatin, rosuvastatin, and fluvastatin.

1 **39.** The dosage form of claim **19** in which said first drug is pyridoxine
2 hydrochloride, and said second drug is a member selected from the group consisting of
3 atorvastatin and simvastatin.

1 **40.** The dosage form of claim **19** in which said second drug is a member
2 selected from the group consisting of metformin hydrochloride, vancomycin hydrochloride,
3 captopril, erythromycin lactobionate, ranitidine hydrochloride, sertraline hydrochloride,
4 ticlopidine hydrochloride, amoxicillin, cefuroxime axetil, cefaclor, clindamycin,
5 doxifluridine, tramadol, fluoxetine hydrochloride, ciprofloxacin hydrochloride, gancyclovir,
6 bupropion, lisinopril, cefaclor, saquinavir, ritonavir, nelfinavir, clarithromycin, azithromycin,
7 ceftazidime, cyclosporin, digoxin, paclitaxel, iron salts, topiramate, and ketoconazole.

1 **41.** The dosage form of claim **19** in which said second drug is a member
2 selected from the group consisting of lisinopril, enalapril, captopril, fosinopril, quinapril,
3 ramipril, and benazepril.

1 **42.** The dosage form of claim **19** in which said second drug is a member
2 selected from the group consisting of losartan, valsartan, candesartan, irbesartan, telmisartan,
3 and eprosartan.

1 **43.** The dosage form of claim **19** in which said first drug is a sulfonylurea
2 selected from the group consisting of glimepiride, glyburide, and glipizide, and said second
3 drug is metformin hydrochloride.

1 **44.** The dosage form of claim **19** in which said first drug is glimepiride and
2 said second drug is metformin hydrochloride.

1 **45.** The dosage form of claim **19** in which said first drug is glyburide and
2 said second drug is metformin hydrochloride.

1 **46.** The dosage form of claim **19** in which said first drug is glipizide and
2 said second drug is metformin hydrochloride.